Thomas P. Koestler, Ph.D.
Vice President,
Global Head

Novartis Pharmaceuticals Corporation
Drug Regulatory Affairs/
Clinical Safety & Epidemiology
59 Route 10
East Hanover, NJ 07936-1080

Tel 973 781 5757
Fax 973 781 5544
Email thomas.koestler@pharma.novartis.com

NOVARTIS

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Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Drive, Room 1-23
Rockville, MD 20857

Subject: Response to Site Specific Stability issues in the Draft Guidance to Industry: Stability Testing of Drug Substances and Drug Products, (Federal Register, Monday, June 8, 1998, Docket # 98D-0362)

Novartis Pharmaceuticals Corporation ("Novartis") appreciates the opportunity to comment on the important issue of Site-Specific Stability requirements which are being proposed in the June 8, 1998 Guidance for Industry Stability Testing of Drug Substances and Drug Products draft guidance document.

Historical review within the former Sandoz and Ciba-Geigy and current Novartis organizations NDA files has revealed the fact that almost 30 New Drug Applications have been approved within our company since January 1, 1989 (approximately 10 years). These approvals include the complete spectrum of dosage form types (tablets/capsules to transdermal systems). In addition, several active ingredients have been successfully transferred to various facilities (post approval) during the same time period. Finally, as per the recent merger to form Novartis, a major site transfer program (post approval) has been initiated, and is currently ongoing within our organization. Considering these three significant and ongoing events, we at Novartis feel quite confident in our ability to evaluate the needs for Site-Specific Stability studies.

At Novartis, we are assured that the internal process validation activities that are being performed by the transfer coordinators, as well as the FDA Field Inspectors who are overseeing these activities, have the greatest impact on a successful site transfer. These internal coordinators employ the use of high standards, which are needed in a typical process validation protocol. Implementation of these standards will assure a "trouble free" site transfer. These transfers are currently being performed by Novartis (pre or post approval) on a continuous basis.

Novartis feels very strongly that once a material has been demonstrated to be the "same", whether it is manufactured at site "one" or "two", it is extremely unlikely that a stability study will uncover an unexpected problem, as stability is characteristic of a material, not a site.

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Novartis feels confident about this conclusion which is based upon having a complete and thorough knowledge of the manufacturing systems that are being employed at both sites.

In addition, the revised FDA proposal that was made available to industry on March 29, 1999 provides little (if any) regulatory relief to the June 8, 1998 draft stability guideline proposal.

Novartis is therefore certain that based upon our history of successful substance and product transfers with no stability failures, (over 50 total US transfers with many more performed by our parent company Novartis Pharma, AG in Basle, Switzerland) over the past 10 years, (pre- and post approval), that the proposed additional requirements which FDA is considering, would be unreasonable, unnecessarily burdensome and constitute an additional expensive and time-consuming hurdle for industry during the drug development process. This position applies to both drugs and well characterized biologics. Novartis is therefore opposed to the incorporation of Site-Specific Stability requirements into the finalized version of the stability guideline.

Thank you for the opportunity to comment. If you should have any questions, please contact Dr. Thomas Koestler at (973) 781-5757 or Robert Clark at (973) 781-7005.

Sincerely,

Adrian L. Koch

for Thomas Koestler, PhD
Vice President, Global Head
Drug Regulatory Affairs